

**REMARKS****1. Preliminary Remarks****a. Status of Claims**

Claims 69-72, 89-96 are pending and under active consideration. Claims 69-72 are allowed.

Claims 89 and 96 are amended. Claims 90, 91, 94, and 95 are canceled. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of this application. Upon entry of the amendments, claims 69-72, 89, 92, 93, and 96 will be pending and under active consideration.

**b. Amendment to the Claims**

In order to expedite prosecution and without prejudice to seeking claims of similar scope in a continuing application, Applicant has canceled claims 90, 91, 94, and 95 without prejudice. Claim 89 has been amended in part (c), which is now directed to an isolated nucleic acid consisting of X nucleotides wherein the sequence of the nucleic acid comprises a sequence at least 80% identical to Y consecutive nucleotides of SEQ ID NO: 2 or 9, or an RNA encoded by Y consecutive nucleotides of SEQ ID NO: 2 or 9, wherein X= 19 to 140, Y $\geq$ 19, and X $\geq$ Y. Support for amended claim 89 can be found throughout the specification, for example, paragraph 0049.

Claim 96 have been amended and is now directed to a vector comprising a heterologous sequence, wherein the heterologous sequence consists of the sequence of the nucleic acid of claims 69-72, 89, 92, 93, and 96. Support for amended claim 96 can be found throughout the specification, for example, paragraph 0039. One of ordinary skill in the art would recognize that features other than the heterologous sequence would be necessary for a functional vector.

**2. Patentability Remarks**

On pages 2-4 of the Office Action, the Examiner rejects claims 89-91 and 96 under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. Specifically, the Examiner asserts that the limitations “a sequence 68.2% identical to (a) or (b),” “a sequence at least 81.9% identical to (a) or (b),” and “a sequence at least 91.0% identical to (a) or (b)” lack support in the disclosure. Applicant respectfully traverses.

As acknowledged by the Examiner on page 4 of the Office Action, the specification describes that miRNAs can bind to target genes with less than 100% complementary, but asserts that the specification does not appear to provide a description sufficient to support a genus of molecules now encompassed by the claims. Applicant disagrees with regard to sufficient description. As discussed in our response filed June 11, 2007, the specification provides numerous examples of the claimed miRNAs as set forth in SEQ ID NOS: 2 and 9 binding target genes with less than 100% complementarity. For example, Table 7, lines 188035-188829 of the specification shows examples of the claimed miRNAs sequences as set forth in

SEQ ID NOS: 2 and 9 binding various target gene sequences with 68.2%, 81.9%, and 91.0% complementarity (See Appendix A).

The Examiner however states on page 3 of the Office Action that a text search of “68.2%,” “81.9%,” and “91.0%” was unsuccessful. Applicant submits that the alignments shown in Table 7 provide the inherent written descriptive support of these percent variants by calculating the percentage of the number of bases that align between the miRNA sequence and the target gene sequence. One of skill in the art can reasonably conclude that the inventor had possession of the claimed invention by the alignments described in Table 7.

Nevertheless, in order to expedite prosecution, claim 89 has been amended as described above because the specification does clearly provide textual support at paragraph 0049 for at least 80% variants of the claimed miRNA sequences as set forth in SEQ ID NOS: 2 and 9 that bind and repress expression of mRNA transcripts of particular target genes. As discussed above, claims 90 and 91 have been canceled without prejudice and claim 96 draws its dependency in part from claim 89. In view of the foregoing amendment and remarks, Applicant respectfully request that the rejection of claims 89-91 and 96 under 35 U.S.C. §112, first paragraph for allegedly lacking proper written description support has been overcome and should be withdrawn.

### 3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification of this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

POL SINELLI SHUGHART PC

Dated: March 12, 2009

On behalf of:      Teddy C. Scott, Jr., Ph.D.  
                            Registration No. 53,573

By: /Paul A. Jenny/  
Paul A. Jenny  
Registration No. 59014  
Customer No. 37808

POLGINELLI SHUGHART PC  
180 N. Stetson Ave., Suite 4525  
Chicago, IL 60601  
312.819.1900 (main)  
312.602.3955 (E-fax)  
312.873.3613 (direct)

## APPENDIX A

Table 7, lines 188035-188829 disclose that the miRNA GAM3298 (SEQ ID NO: 2) is capable of binding to sites within 326 target gene mRNAs. Table 7 further discloses that 15 out of 22 nucleotides (68.2%) of GAM3298 are sufficient for binding target mRNAs. For example, 68.2% of the residues of SEQ ID NO: 2 are capable of targeting mRNAs of the genes HIP1 and ADCY1, as follows:

GAM	NAME	GAM RNA	TARGET	TARGET	UTR	TARGET	BS-SEQ	BINDING-SITE DRAW	GAM
SEQUENCE		REF-ID					(UPPER:GAM; LOWER:TARGET)	POS	POS
GAM3298		AAAGTGCTCAT	HIP1	NM_005338.3	3	ACGCCCTGTAATCC CAGCACTTT	CATAG AAAGTGCT TTTCACCGA CCCTA	AG TGCAGGT ATGTCCG CA	A
GAM3298		AAAGTGCTCAT	ADCY1	NM_021116.1	3	TGTTTGGACTATA CTTT	GCTC AAAGT TTTCA	GG ATAGTGCA TATCACGT ---- TT	A

Table 7 also discloses that the mRNA GAM2608 (SEQ ID NO: 9) is capable of binding to sites within 117 target gene mRNAs. Table 7 further discloses that 15 out of 22 nucleotides (68.2%) of GAM2608 are sufficient for binding target gene mRNAs. For example, 68.2% of the residues of SEQ ID NO: 9 are capable of targeting mRNAs of the genes CALCB and EGR4, as follows:

GAM2608	TAAGGTGCA	TAC	CALCB	NM_000728.2	3	TAATTGCCCTGCT ACCTTT	TCTAGT AAAGTGCA TTCCACGT	GCAGTTA CGTTAAC	A
GAM2608	TAAGGTGCA	TAC	EGR4	NM_001965.1	3	TAACTGCAACACGC CCCACGCCCTC	T CATCTA-- AAGGTG TTCCGC C	GTCAGTTA CACGTCAAT ACCCCGCA	A

Table 7 discloses that 18 out of 22 nucleotides (81.9%) of the miRNA GAM3298 (SEQ ID NO: 2) are sufficient for binding target gene mRNAs. For example, 81.9% of the residues of SEQ ID NO: 2 are capable of targeting mRNAs of the genes ABCC3 and ADSL, as follows:

GAM3298	AAAGTGCTCAT	ABCC3	NM_020037.1	3	TACCTGCACTGTC CTGACCACATCGAC	AAA GTGC CACG ---- CTACC	TCA AGT GTCACGTTCCAT CCT	TAGTGAGGTA GTCACGTTCCAT	A
GAM3298	AAAGTGCTCAT	ADSL	NM_000026.1	3	TTACCTTAAATTAGTACAGCAC	CA-- AAAGTGCT TTTCACCGA CATG	GC-- TAGT ATTAA AAT	AGGTAG TCCATT	A

Table 7 also discloses that 18 out of 22 nucleotides (81.9%) of the miRNA GAM2608 (SEQ ID NO: 9) are sufficient for binding target gene mRNAs. For example, 81.9% of the residues of SEQ ID NO: 9 are capable of targeting mRNAs of the genes ABCC3 and CASP3, as follows:

GAM2608	TAAGGTGCATC ABCC3	NM_020038.1	3	TAGCAAACACTGG GGGCACCTTA	AT CA-	A
	TAGTGCAGTTA				TAAGGTGC CTAGTG GTTA ATTCCACG GGTCAC CGAT GG	AAA
GAM2608	TAAGGTGCATC CASP3	NM_032991.1	3	TAACTGCATTTTA GACCATTAT	TA CA --	A
	TAGTGCAGTTA				AGGTG TCTA GTGCAGTTA TTTAC AGAT TACGTCAAT TA C- TT	

Table 7 discloses that 20 out of 22 nucleotides (91.0%) of the miRNA GAM3298 (SEQ ID NO: 2) are sufficient for binding target gene mRNAs. For example, 91.0% of the residues of SEQ ID NO: 2 are capable of targeting mRNAs of the genes ASTN and MECP2, as follows:

GAM3298	AAAGTGCCTCAT ASTN	NM_045113.2	3	ATGCCAGGGCCTG ATGTAAGCACTT	-- - A- G	A
	AGTCAGGAGTAG				AAAGTGC CAT AGTGC GGTA TTTCACGA GTA TCGGG CCGT AT G GA A	
GAM3298	AAAGTGCCTCAT MECP2	NM_004992.2	3	TTATTTGCCTAT TGAGTCTTC	- - -	A
	AGTCAGGAGTAG				AAG GCTCA TAGTGCAGGTAG TTC TGAGT ATCACGTTTATT C - T	

Table 7 also discloses that 20 out of 22 nucleotides (91.0%) of the miRNA GAM2608 (SEQ ID NO: 9) are sufficient for binding target gene mRNAs. For example, 91.0% of the residues of SEQ ID NO: 9 are capable of targeting mRNAs of the genes MAP4K5 and MMP26, as follows:

GAM2608	TAAGGTGCATC MAP4K5	NM_006575.2	3	AAACTGCACTATG ATTGCTTAA	C - - A	A
	TAGTGCAGTTA				TAAGGTG ATC TAGTGCAGTT ATTTCGT TAG ATCACGTCAA T T A	
GAM2608	TAAGGTGCATC MMP26	NM_021801.2	3	AACTGAAAGCACT AGAGCAGCCTTG	- A ----	A
	TAGTGCAGTTA				TAAGG TGC TCTAGTGC GTTCC ACG AGATCACG G - AAAG TCAA	